

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

United States Patent and Trademark
Office
(Box PCT)
Crystal Plaza 2
Washington, DC 20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 07 March 1997 (07.03.97)	
International application No. PCT/US96/09604	Applicant's or agent's file reference ISIS-2275
International filing date (day/month/year) 07 June 1996 (07.06.96)	Priority date (day/month/year) 07 June 1995 (07.06.95)
Applicant HEBERT, Normand	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

07 January 1997 (07.01.97)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer M. Abidine
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 730.91.11

PATENT COOPERATION TREATY

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NOTIFICATION CONCERNING
SUBMISSION OF PRIORITY DOCUMENTS

(PCT Administrative Instructions, Section 411)

From the INTERNATIONAL BUREAU

To:

CALDWELL, John, W.
Woodcock Washburn Kurtz Mackiewicz
& Norris
46th floor
One Liberty Place
Philadelphia, PA 19103
ETATS-UNIS D'AMERIQUE

Date of receipt (day/month/year) January 1997 (31.01.97)		IMPORTANT NOTIFICATION	
Date of agent's file reference PCT/US96/09604			
International application No. PCT/US96/09604	International filing date (day/month/year) 07 June 1996 (07.06.96)	Priority date (day/month/year) 07 June 1995 (07.06.95)	
Applicant ISIS PHARMACEUTICALS, INC. et al			

The International Bureau is hereby notified of the date of receipt by the International Bureau of the priority document(s) relating to the

Priority document No.	Priority date	Priority country	Date of receipt of priority document
2,067,311	07 Jun 1995 (07.06.95)	US	07 Jun 1996 (07.06.96)

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

A. Addae-Ruesch

Telephone No.: (41-22) 730.91.11

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF DEFECTS IN
THE INTERNATIONAL APPLICATION

(PCT Articles 3(4)(i) and 14(1) and Rule 28.1)

To

United States Patent and
Trademark Office
Washington, DC

(RO)

in its capacity as receiving Office

Date of mailing
(day/month/year) 10 July 1996 (10.07.96)

International application No.
PCT/US96/09604

International filing date
(day/month/year)
07 June 1996 (07.06.96)

Applicant
ISIS PHARMACEUTICALS, INC.

The International Bureau hereby calls the attention of the receiving Office to the defects in the international application, which are specified on the attached



Annex A



Annex B



Annex C

Additional observations, if necessary:

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Authorized officer

A. Addae Ruesch



Facsimile No. (41-22) 740.14.35

Telephone No. (41-22) 730.91.11

The International Bureau has found the following defects in the international application:

1. As to **signature*** of the international application (Rules 4.15 and 90.4), the request:

- a. ☐ is not signed.
- b. ☐ is not signed by all the applicants.
- c. ☐ is not accompanied by the statement referred to in the check list in Box No. VIII of the request explaining the lack of the signature of an applicant for the designation of the United States of America.
- d. ☒ is signed by what appears to be an agent/common representative but
 - ☐ the international application is not accompanied by a power of attorney appointing him.
 - ☒ the power of attorney accompanying the international application is not signed by all the applicants.
(HERBERT, Normand)
- e. ☐ other (specify):

* All applicants must sign, including inventors if they are also applicants (e.g. where the United States of America is designated)

2. As to indications concerning the **applicant**, the request (Rules 4.4 and 4.5):

- a. ☐ does not properly indicate the applicant's name (specify):
- b. ☐ does not indicate the applicant's address.
- c. ☐ does not properly indicate the applicant's address (specify):
- d. ☐ does not indicate the applicant's nationality.
- e. ☐ does not indicate the applicant's residence.
- f. ☐ other (specify):

3. As to the **language** of some parts of the international application (Rule 12.1):

- a. ☐ the request is not in (one of) the admitted language(s) which is (are): _____
- b. ☐ the text matter of the drawings is not in (one of) the admitted language(s) which is (are): _____
- c. ☐ the abstract is not in (one of) the admitted language(s) which is (are): _____

4. The **title** of the invention:

- a. ☐ is not indicated in Box No. I of the request (Rule 4.1).
- b. ☐ is not indicated at the top of the first sheet of the description (Rule 5.1(a)).
- c. ☐ as appearing in Box No. I of the request is not identical with the title heading the description (Rule 5.1(a)).

PATENT COOPERATION TREATY

PCT

RE

02 SEP 1997

WIPO

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference ISIS-2275	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US96/09604	International filing date (day/month/year) 07 JUNE 1996	Priority date (day/month/year) 07 JUNE 1995
International Patent Classification (IPC) or national classification and IPC IPC(6): C07D 333/06; A61K 31/38 and US Cl.: 549/06; 514/444		
Applicant ISIS PHARMACEUTICALS, INC.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

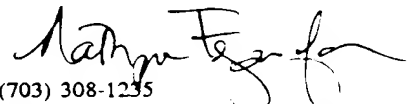
2. This REPORT consists of a total of 4 sheets.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 07 JANUARY 1997	Date of completion of this report 14 AUGUST 1997
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer JOSE DEES  Telephone No. (703) 308-1235

PCTWORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : C07D 333/06, A61K 31/38	A1	(11) International Publication Number: WO 96/40672 (43) International Publication Date: 19 December 1996 (19.12.96)
(21) International Application Number: PCT US96/09604 (22) International Filing Date: 7 June 1996 (07.06.96) (30) Priority Data: 08/483,311 7 June 1995 (07.06.95) US (60) Parent Application or Grant (63) Related by Continuation US 08/483,311 (CIP) Filed on 7 June 1995 (07.06.95) (71) Applicant (for all designated States except US): ISIS PHARMACEUTICALS, INC. [US/US]; 2280 Faraday Avenue, Carlsbad, CA 92008 (US). (72) Inventor; and (75) Inventor/Applicant (for US only): HEBERT, Normand [CA/US]; 1861 Montgomery Avenue, Cardiff, CA 92007 (US). (74) Agents: CALDWELL, John, W. et al.; Woodcock Washburn Kurtz Mackiewicz & Norris, 46th floor, One Liberty Place, Philadelphia, PA 19103 (US).		(81) Designated States: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, ARIPO patent (KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i>
(54) Title: COMBINATORIAL LIBRARIES HAVING AMINODIOL MONOMER SUBUNITS (57) Abstract Combinatorial libraries are constructed to include aminodiol monomer subunits connected by phosphodiester, phosphorothioate, or phosphoramidate linking moieties. Combinatorial libraries of the invention feature a plurality of functional groups attached to backbone and phosphoramidate combinatorial sites.		

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US96/09604

I. Basis of the report

1. This report has been drawn on the basis of (Substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments):

☒ the international application as originally filed.

☒ the description, pages 1-151 , as originally filed.

pages NONE , filed with the demand.

pages NONE , filed with the letter of _____.

pages _____ , filed with the letter of _____.

☒ the claims, Nos. 1-26 , as originally filed.

Nos. NONE , as amended under Article 19.

Nos. NONE , filed with the demand.

Nos. NONE , filed with the letter of _____.

Nos. _____ , filed with the letter of _____.

☒ the drawings, sheets/fig 1-2 , as originally filed.

sheets/fig NONE , filed with the demand.

sheets/fig NONE , filed with the letter of _____.

sheets/fig _____ , filed with the letter of _____.

2. The amendments have resulted in the cancellation of:

☒ the description, pages NONE .

☒ the claims, Nos. NONE .

☒ the drawings, sheets/fig NONE .

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box Additional observations below (Rule 70.2(c)).

4. Additional observations, if necessary:

NONE

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US96/09604

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The question whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

- ☐ the entire international application.
- ☒ claims Nos. 1-26 (in part)

because:

- ☐ the said international application, or the said claim Nos. _ relate to the following subject matter which does not require international preliminary examination (*specify*).

- ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1-26 (in part) are so unclear that no meaningful opinion could be formed (*specify*).

The claims are too broadly formulated to permit a meaningful examination. The examination has been limited to dimer compounds according to structure II, linked via a N-benzyl phosphoramidate linkage, wherein R1 is -C(=O)-CH₂-2thiophenyl; R3 and R4 are each hydrogen and each x is 1.

- ☐ the claims, or said claims Nos. _ are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for said claims Nos. 1-26 (in part).

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US96/09604

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**1. STATEMENT**

Novelty (N)	Claims	<u>1-26 (in part)</u>	YES
	Claims	<u>NONE</u>	NO
Inventive Step (IS)	Claims	<u>1-26 (in part)</u>	YES
	Claims	<u>NONE</u>	NO
Industrial Applicability (IA)	Claims	<u>1-26 (in part)</u>	YES
	Claims	<u>NONE</u>	NO

2. CITATIONS AND EXPLANATIONS

Claims 1-26 (in part) meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the amino diol library of compounds.

Claims 1-26 (in part) meet the criteria set out in PCT Article 33(4), for industrial applicability.

_____ NEW CITATIONS _____

NONE

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US96/09604**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(6) : C07D 333/06; A61K 31/38

US CL : 549/06; 514/444

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 549/06; 514/444

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
NONE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CAS ONLINE

structure search of multiple moieties encompassed by structures I-XI

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, Volume 116, Number 6, issued 23 March 1994, Chen et al., "Analogous Organic Synthesis of Small-Compound Libraries: Validation of Combinatorial Chemistry in Small-Molecule Synthesis", pages 2661-2662, see entire document.	1-26

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
A Document defining the general state of the art which is not considered to be of particular relevance	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
E earlier document published on or after the international filing date	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*G* document member of the same patent family
O document referring to an oral disclosure, use, exhibition or other means	
P document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

22 AUGUST 1996

Date of mailing of the international search report

05 SEP 1996

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

MARY C. CEBULAK

Telephone No. (703) 308-1235

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US96/09604

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 1-26
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

Claims 1-26 are too broadly formulated to permit a meaningful search. The search has been limited to dimer compounds of structure II, linked via a N-benzyl phosphoramidate linkage, wherein R1 is -C(=O)-CH₂-2-thiophenyl; R3 and R4 are each hydrogen; and each x is 1.
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐

The additional search fees were accompanied by the applicant's protest.

☐

No protest accompanied the payment of additional search fees.